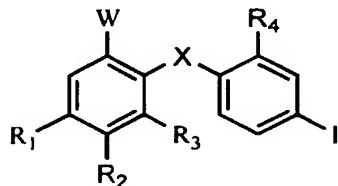


CLAIMS

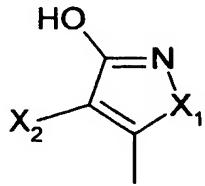
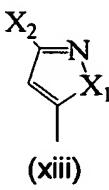
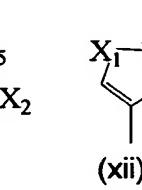
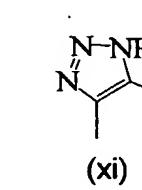
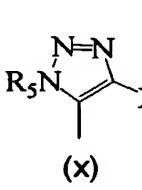
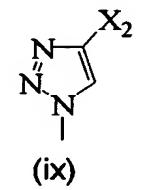
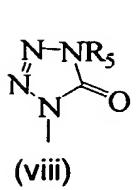
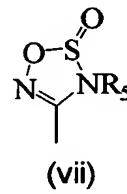
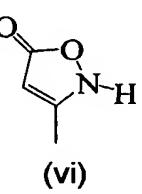
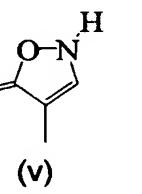
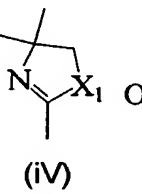
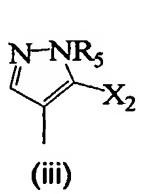
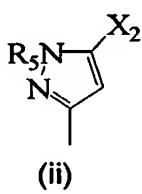
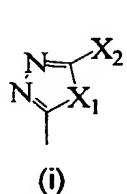
1. A method for treating chronic pain, said method comprising
 administering to a subject in need of such treatment a composition comprising
 5 a MEK inhibitor selected from: a compound of formula (I):



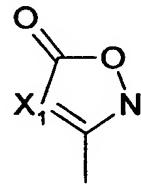
(I)

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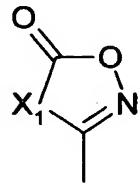
W is one of the following formulae (i) – (xiii):



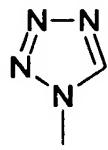
(xiv)



(xv)



(xvi)



(xvii)

15

X1 is O, S, or NR5;

X₂ is OH, SH, or NH_E;

each of R_E and R_F is H or C₁₋₄ alkyl;

5

each of R₁ and R₂ is independently selected from H, F, NO₂, Br and Cl; R₁ can also be SO₂NR_GR_H, or R₁ and R₂ together with the benzene ring to which they are attached constitute an indole, isoindole, benzofuran, benzothiophene, indazole, benzimidazole, or benzthioazole;

10

R₃ is H or F;

each of R_G, R_H, and R₄ is independently selected from H, Cl and CH₃;

15

R₅ is H or C₃₋₄ alkyl; and

wherein each hydrocarbon radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, hydroxyl, amino, (amino)sulfonyl, and NO₂; and

20

wherein each heterocyclic radical above is optionally substituted with between 1 and 3 substituents independently selected from halo, C₃₋₄ alkyl, C₃₋₆ cycloalkyl, C₃₋₄ alkenyl, C₃₋₄ alkynyl, phenyl, hydroxyl, amino, (amino)sulfonyl, and NO₂, wherein each substituent alkyl, cycloalkyl, alkenyl,

25

alkynyl or phenyl is in turn optionally substituted with between 1 and 2 substituents independently selected from halo, C₁₋₂ alkyl, hydroxyl, amino, and NO₂;

or a pharmaceutically acceptable salt or C₁₋₈ ester thereof.

30

2. The method of claim 1, wherein said chronic pain is selected from neuropathic pain, idiopathic pain, and pain associated with chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.
3. The method of claim 2, wherein said chronic pain is a type of neuropathic pain.
4. The method of claim 3, wherein said neuropathic pain is associated with one of the following: inflammation, postoperative pain, phantom limb pain, burn pain, gout, trigeminal neuralgia, acute herpetic and postherpetic pain, causalgia, diabetic neuropathy, plexus avulsion, neuroma, vasculitis, 10 viral infection, crush injury, constriction injury, tissue injury, limb amputation, post-operative pain, arthritis pain, and any other nerve injury between the peripheral nervous system and the central nervous system, inclusively.
5. The method of claim 2, wherein said chronic pain is associated with 15 chronic alcoholism, vitamin deficiency, uremia, or hypothyroidism.
6. The method of claim 2, wherein said chronic pain is associated with idiopathic pain.
- 20 7. The method of claim 1, wherein said chronic pain is associated with inflammation.
8. The method of claim 1, wherein said chronic pain is associated with arthritis.
- 25 9. The method of claim 1, wherein said chronic pain is associated with post-operative pain.
- 30 10. The method of claim 1, wherein R₁ is bromo or chloro.

11. A method of claim 1, wherein R₂ is fluoro.
12. A method of claim 1, wherein R₃ is H.
5
13. A method of claim 12, wherein each of R₂ and R₃ is H.
14. A method of claim 1, wherein each of R₂ and R₃ is fluoro.
- 10 15. A method of claim 14, wherein R₁ is bromo.
16. A method of claim 14, wherein R₁ is fluoro.
17. A method of claim 1, wherein R₂ is nitro.
15
18. A method of claim 16, wherein R₃ is H.
19. A method of claim 1, wherein R₄ is chloro.
- 20 20. A method of claim 1, wherein R₄ is methyl.
21. A method of claim 1, wherein R₅ is H.
22. A method of claim 1, wherein R₅ is CH₃.
25
23. A method of claim 1, wherein X₁ is O or S.
24. A method of claim 1, wherein X₁ is NH or NCH₃.
- 30 25. A method of claim 1, wherein X₂ is OH, SH, or NH₂.
26. A method of claim 1, wherein X₂ is NHCH₃ or OH.

27. A method of claim 1, wherein said MEK inhibitor has a structure selected from: [5-fluoro-2-(1H-tetrazol-5-yl)-phenyl]-(4-iodo-2-methyl-phenyl)-amine; [2,3-difluoro-6-(1H-tetrazol-5-yl)-phenyl]-(4-iodo-2-methyl-phenyl)-amine; (4-iodo-2-methyl-phenyl)-[2,3,4-trifluoro-6-(1H-tetrazol-5-yl)-phenyl]-amine; [4-bromo-2,3-difluoro-6-(1H-tetrazol-5-yl)-phenyl]-(4-iodo-2-methyl-phenyl)-amine; [5-fluoro-4-nitro-2-(1H-tetrazol-5-yl)-phenyl]-(4-iodo-2-methyl-phenyl)-amine; [2-(4,4-dimethyl-4,5-dihydro-oxazol-2-yl)-5-fluoro-phenyl]-(4-iodo-2-methyl-phenyl)-amine; [6-(4,4-dimethyl-4,5-dihydro-oxazol-2-yl)-2,3-difluoro-phenyl]-(4-iodo-2-methyl-phenyl)-amine; [6-(4,4-dimethyl-4,5-dihydro-oxazol-2-yl)-2,3,4-trifluoro-phenyl]-(4-iodo-2-methyl-phenyl)-amine; [4-bromo-6-(4,4-dimethyl-4,5-dihydro-oxazol-2-yl)-2,3-difluoro-phenyl]-(4-iodo-2-methyl-phenyl)-amine; [2-(4,4-dimethyl-4,5-dihydro-oxazol-2-yl)-5-fluoro-4-nitro-phenyl]-(4-iodo-2-methyl-phenyl)-amine; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]thiadiazol-2-ol; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]thiadiazol-2-ol; 5-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]thiadiazol-2-ol; 5-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]thiadiazol-2-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-[1,3,4]thiadiazol-2-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]oxadiazol-2-ol; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]oxadiazol-2-ol; 5-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]oxadiazol-2-ol; 5-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]oxadiazol-2-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-[1,3,4]oxadiazol-2-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-[1,2,4]triazol-3-ol; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-[1,2,4]triazol-3-ol; 5-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-[1,2,4]triazol-3-ol; 5-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-[1,2,4]triazol-3-ol; and 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-4H-[1,2,4]triazol-3-ol.

trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-[1,2,4]triazole-3-thiol; 5-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-[1,2,4]triazole-3-thiol; and 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-4H-[1,2,4]triazole-3-thiol.

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29. A method of claim 1, wherein said MEK inhibitor has a structure selected from: 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 5-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 5-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-isothiazol-3-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 5-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 5-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-isoxazol-3-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-pyrazol-3-ol; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-pyrazol-3-ol; 5-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-pyrazol-3-ol; 5-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-pyrazol-3-ol; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-1H-pyrazol-3-ol; 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 4-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 4-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 4-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isothiazol-3-ol; 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-isothiazol-3-ol; 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 4-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 4-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 4-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-isoxazol-3-ol; 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-isoxazol-3-ol; 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-pyrazol-3-ol; 4-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-pyrazol-3-ol;

methyl-phenylamino)-phenyl]-1-methyl-1H-pyrazol-3-ol; 1-methyl-4-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-pyrazol-3-ol; 4-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1-methyl-1H-pyrazol-3-ol; and 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-1-methyl-1H-pyrazol-3-ol.

1H-[1,2,3]triazol-4-ol; 1-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-[1,2,3]triazol-4-ol; 1-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-[1,2,3]triazol-4-ol; 1-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-1H-[1,2,3]triazol-4-ol; and 1-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-1H-[1,2,3]triazol-4-ol.

31. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 3-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-2H-isoxazol-5-one; 3-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-2H-isoxazol-5-one; 3-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-2H-isoxazol-5-one; 3-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-2H-isoxazol-5-one; 3-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-2H-isoxazol-5-one; [5-fluoro-2-(2-oxo-2,3-dihydro-2l>4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl]-[4-iodo-2-methyl-phenyl]-amine; [2,3-difluoro-6-(2-oxo-2,3-dihydro-2l>4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl]-[4-iodo-2-methyl-phenyl]-amine; (4-iodo-2-methyl-phenyl)-[2,3,4-trifluoro-6-(2-oxo-2,3-dihydro-2l>4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl]-amine; [4-bromo-2,3-difluoro-6-(2-oxo-2,3-dihydro-2l>4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl]-[4-iodo-2-methyl-phenyl]-amine; [5-fluoro-4-nitro-2-(2-oxo-2,3-dihydro-2l>4-[1,2,3,5]oxathiadiazol-4-yl)-phenyl]-[4-iodo-2-methyl-phenyl]-amine; 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-isoxazol-5-one; 4-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-isoxazol-5-one; 4-[3,4,5-trifluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-isoxazol-5-one; 4-[5-bromo-3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4H-isoxazol-5-one; and 4-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-5-nitro-phenyl]-4H-isoxazol-5-one.

32. The method of claim 1, wherein said MEK inhibitor has a structure selected from: 2,4-bis-(2-chloro-4-iodo-phenylamino)-3fluoro5-nitro-benzoic acid; 5-[3,4difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]oxadiazol-2-ylamine; 5-[4-fluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]oxadiazol-2-ol; (2,3-difluoro-6-[1,3,4]oxadiazol-2-yl-phenyl)(-(4-iodo-2-

methyl-phenyl)-amine; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-[1,3,4]oxadiazole-2-thiol; 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4*H*-[1,2,4]triazole-3-ylamine; and 5-[3,4-difluoro-2-(4-iodo-2-methyl-phenylamino)-phenyl]-4*H*-[1,2,4]triazole-3-thiol.

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33. The method of claim 1, wherein said MEK inhibitor has the structure: 2,4-bis-(2-chloro-4-iodo-phenylamino)-3-fluoro-5-nitro-benzoic acid.